RECEIVED
CENTRAL FAX CENTER
DEC 21 2006

Applicants: Mark Ledeboer et al.
Application No.: 10/700,333

REMARKS

The Claim Amendments

Applicants have amended claim 1 to more precisely define variable R^1. Support may be found in originally-filed claims 1 and 4 and in Tables 1-8 on pages 48-58 of the specification. Applicants have amended claims 5, 45 and 46 to correct typographical errors. Support for these amendments may be found in the originally filed claims and throughout the specification. Applicants have amended claims 56, 57 and 58 to more precisely define the claimed invention. Support may be found in originally-filed claims 56, 58 and 59 and in paragraph [00211] on page 74 of the specification. Applicants have canceled claims 4 and 59. None of the amendments contain new matter. Their entry is requested.

Applicants reserve the right to pursue canceled subject matter in this application or in future continuing or divisional applications.

The Response

The Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 4-6 and 40-54 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner states that there is no antecedent basis in claim 1 for the limitation of R^1 in claims 4-6 and 40-54 as an optionally substituted phenyl, cyclohexyl, cyclopentyl, pyridyl, morpholino, piperazinyl or piperidinyl group.

Applicants have amended claim 1 to recite that R^1 is an optionally substituted phenyl, cyclohexyl, cyclopentyl, pyridyl, morpholino, piperazinyl, or piperidinyl group, thereby obviating this rejection.

The Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner has rejected claims 57-59 under 35 U.S.C. §112, first paragraph, because the Examiner, while acknowledging that the specification enables a method of treatment of rheumatoid arthritis, contends that the specification does not

reasonably provide enablement for a method of treating or lessening the severity or prevention of other diseases or conditions recited in the claims. Applicants traverse with respect to the amended claims.

Applicants have amended claim 57 to recite a method of inhibiting JAK kinase activity in a biological sample *in vitro*. Methods of inhibiting JAK kinase activity in a biological sample *in vitro* would be known to one skilled in the art in view of the specification. See, e.g., paragraph [00245] on page 83. Applicants have also canceled claim 59 and amended claim 58 to recite specific diseases that can be treated using compounds of the invention. The Examiner has acknowledged that treating rheumatoid arthritis with compounds of the invention are enabled. Methods of treating or lessening the severity of allergic or type I hypersensitivity reaction, asthma, transplant rejection and familial amyotrophic lateral sclerosis (FALS) were also enabled by the specification at the time of filing. The specification teaches that inhibiting JAK3 prevents allergic or type I hypersensitivity reactions, including anaphylaxis. See, e.g., [008] on pages 2-3 of the specification and the references cited therein. In addition, a JAK3 inhibitor has been shown to be effective in inhibiting asthma in a mouse model. See, e.g., Malaviya et al., J. Pharmacol. Exp. Ther. 295:912-26, 2000. Further, in a well-known organ transplantation animal model (a rat heart allograft model), administration of inhibitors of JAK3 provided dose-dependent survival for animals. See, e.g., [009] on page 3 of the specification and the reference cited therein. A JAK3 inhibitor also has been shown to inhibit kidney allograft rejection in a non-human primate. See, e.g., Changelian et al., Science 302:875-8, 2003. In addition, the specification teaches that administration of a JAK3 inhibitor increases survival in a mouse model of FALS. See, e.g., paragraph [0011] of the specification and Trieu et al., Biochem. Biophys. Res. Comm. 267:22-25, 2000. Thus, provided with the teachings of the specification and the general knowledge of one skilled in the art at the time the invention was made, an artisan could treat or lessen the severity of a number of diseases or disorders using compounds of the instant invention without undue experimentation.

Applicants: Mark Ledeboer et al.
Application No.: 10/700,333

The Rejection Under 35 U.S.C. §102(b)

The Examiner has rejected claims 1, 7, 10-16, 19, 20, 22, 24, 25, 28, 37, 38 and 55-59 under 35 U.S.C. §102(b) as allegedly being anticipated by Nuss et al., WO 02/20495 (hereafter "the '495 application"). Applicants traverse in light of the amended claims.

The '495 application requires a three-atom linker between the amino group on the pyridine or pyrimidine and the aryl or heteroaryl group, while the instant claims, as amended, recite that R^1 is directly linked to the amino group at the 2-position of the pyrimidine ring. Thus, the '495 application does not anticipate the claimed invention.

The Rejection Under 35 U.S.C. §103(a)

The Examiner has rejected claims 1, 7-29, 31, 32, 34, 35, 37, 38 and 55-59 under 35 U.S.C. §103(a) as allegedly being obvious over the '495 application. The Examiner states that the '495 application does not exemplify all compounds generically embraced in formula I and formula IV, but teaches the equivalency of various compounds exemplified with those generically claimed. Applicants traverse in light of the amended claims.

As discussed above, the '495 application requires a linker between the amino group and the aryl or heteroaryl group, and neither teaches nor suggests the instantly claimed compounds or methods of using these compounds. Thus, the '495 application does not render obvious the claimed invention.

The Double Patenting Rejections

The Examiner has provisionally rejected claims 1, 4-29, 31, 32, 34, 35, 37, 38 and 40-59 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-24 of copending application 10/702,113 (hereafter "the '113 application"). The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of instant claims substantially overlap with claims 1-24 of the '113 application.

The Examiner has provisionally rejected claims 1, 4-29, 31, 32, 34, 35, 37, 38 and 40-59 on the grounds of nonstatutory obviousness-type double patenting as being

Applicants: Mark Ledeboer et al.
Application No.: 10/700,333

unpatentable over claims 1-60 of copending application 10/638,784 (hereafter "the '784 application").[1] The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of instant claims substantially overlap with claims 1-60 of the '784 application.

Applicants stand ready to provide a terminal disclaimer over each of the '113 application and '784 application upon indication of allowable subject matter.

Conclusion

Applicants request that the Examiner enter the above amendments, consider the accompanying arguments, and allow the claims to pass to issue. Should the Examiner deem expedient a telephone discussion to further the prosecution of the above application, applicants request that the Examiner contact the undersigned at his convenience.

Respectfully submitted,

Karen E. Brown

Karen E. Brown
Reg. No. 43,866
Attorney for Applicants
c/o Vertex Pharmaceuticals Incorporated
130 Waverly Street
Cambridge, Massachusetts 02139
Tel: (617) 444-6168
Fax: (617) 444-6483

[1] Applicants believe that the Examiner meant to recite application 10/639,784.